Electrical synapses: **Beyond speed and synchrony to computation**

Eve Marder

Classically, electrical synapses were thought only to increase the speed and synchrony of neural activity, but recent results suggest that rectifying electrical synapses can act as coincidence detectors, and regulation of the strength of other electrical synapses can enhance oscillatory or asynchronous neural activity.

Address: Volen Center and Biology Department, MS 013, Brandeis University, 415 South St., Waltham, Massachusetts 02454-9110, USA.

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Conventional wisdom — if there is any such thing in neuroscience — holds that electrical synapses provide speed and synchrony in neuronal networks [1]. Like many other tenets of conventional wisdom, this simplistic statement is partially true some of the time. The picture has been complicated by recent results, which have revealed additional computational roles for electrical coupling and shown that it can have rather subtle effects that are not intuitively obvious.

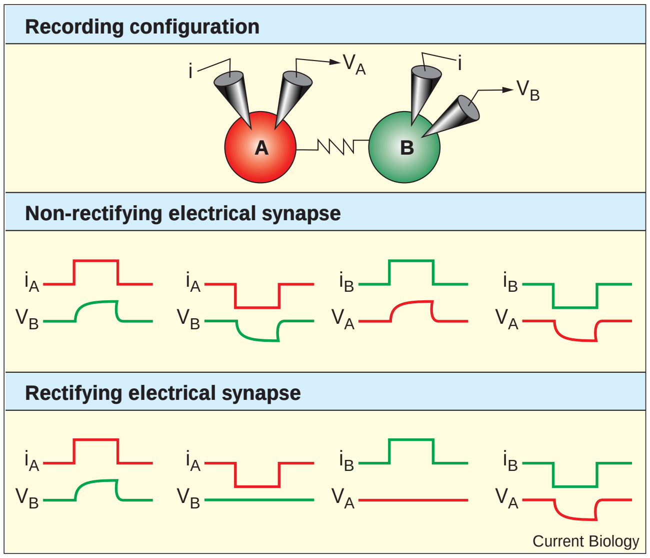
Rectifying, or voltage-sensitive, electrical synapses preferentially pass current in only one direction (Figure 1) [1]. The classic demonstration of electrical transmission [2] at the synapse between the lateral giant and motor giant neurons of the crayfish showed that depolarizing signals, such as action potentials, preferentially travel from the lateral giant neuron to the motor giant neuron, whereas hyperpolarizing pulses of current pass preferentially in the opposite, 'antidromic' direction. Edwards *et al.* [3] now argue that rectifying electrical synapses in convergent neuronal pathways are ideally constituted to function as coincidence detectors.

Coincidence detection is important for numerous functions in the brain, most notably in the auditory system, where sound localization is achieved by coincidence detectors of astonishing precision [4]. There are a number of mechanisms, including spatial spread of inputs on dendrites [5], that can be invoked to construct circuits in which postsynaptic activity requires the precise timing of two or more presynaptic inputs. Edwards *et al.* [3] use a computational model and provide experimental evidence to demonstrate that coincidence detection can be effected by rectifying electrical synapses from several presynaptic sensory neurons that evoke excitatory postsynaptic potentials in the lateral giant neuron of the crayfish.

The key to understanding the model presented in Edwards *et al.* [3] is what happens at a single rectifying synapse in response to a single presynaptic action potential (Figure 2). When both the presynaptic and postsynaptic neurons are at rest, there is little voltage difference across the junction, so its conductance is low and there is little driving force across that small junctional conductance. When the presynaptic neuron fires an action potential it produces a large voltage difference across the junction. The junctional conductance consequently increases rapidly, and the large voltage difference across that large conductance produces a large inward synaptic current in the postsynaptic neuron which generates an excitatory postsynaptic potential (Figure 2).

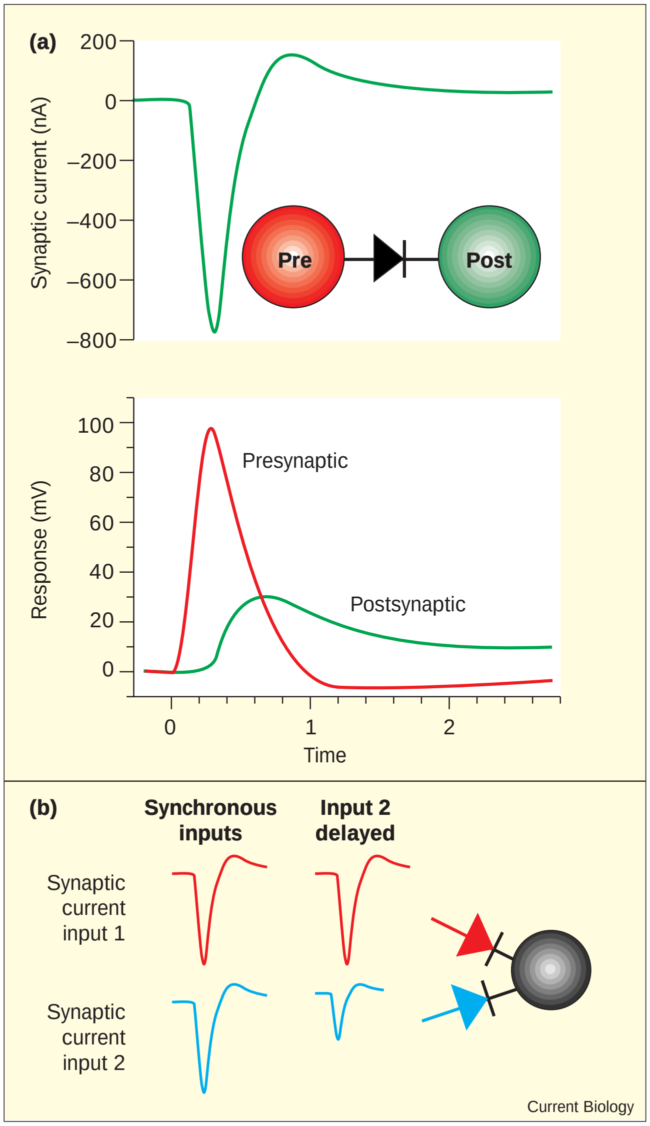
As the presynaptic neuron repolarizes to the resting state, there is a point at which the presynaptic and postsynaptic neurons are at the same potential, and no current flows through the still open junctional conductance. The sign of the synaptic current changes as the membrane potential of the presynaptic neuron falls below that of the postsynaptic neuron, producing an outward current that truncates the falling phase of the excitatory postsynaptic potential in the postsynaptic neuron. As the voltage across the junction

Figure 1



Rectifying and non-rectifying electrical synapses. The diagram at the top shows the configuration for recording the activities of two electrically-coupled neurons, A and B. In each cell, one electrode records the membrane potential (V) and the other electrode injects current (i). The top set of recordings shows typical results for a non-rectifying synapse, where current is passed equally well in both directions; the bottom set of recordings shows typical results for a rectifying electrical synapse.

Figure 2



Rectification provides a mechanism for coincidence detection in the crayfish. **(a)** The top trace is the postsynaptic current evoked by a presynaptic action potential, and the bottom traces show the presynaptic and postsynaptic potential changes. Note that the postsynaptic potential – the excitatory postsynaptic potential – lags both the presynaptic action potential and the postsynaptic current. Note also that the postsynaptic current has a large inward (downward) phase and a late outward (upward) phase. (Modified from [3].) **(b)** Presynaptic inputs 1 and 2 make rectifying electrical synapses with a single postsynaptic neuron. When inputs 1 and 2 fire simultaneously, the postsynaptic currents are both large; when input 1 precedes input 2 by a short time – here 0.25 milliseconds – the postsynaptic current evoked by input 2 is much reduced. (Modified from [3].)

becomes low and reversed in sign, the junctional conductance starts closing, and the size and time course of the outward current that contributes to the truncation of the excitatory postsynaptic potential depends on the rate at which the junctional conductance closes.

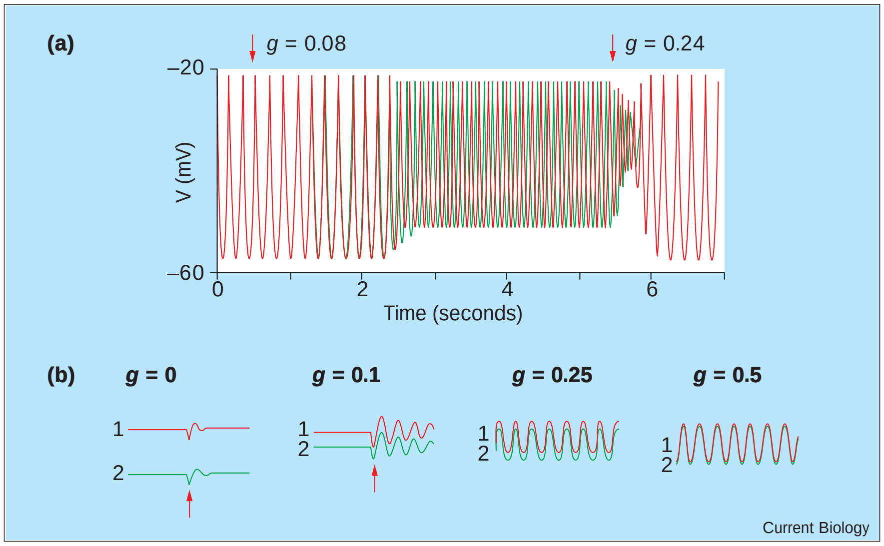
When two presynaptic neurons fire action potentials simultaneously, they are both initially very depolarized relative to the postsynaptic neuron; the inward synaptic currents resulting from the rectifying junctions are therefore both large, and the postsynaptic currents sum. When there is a short delay between the presynaptic action potentials in two neurons, however, the excitatory postsynaptic potential resulting from the first cell's action potential decreases the voltage difference between the postsynaptic neuron and the second presynaptic neuron. The second spike thus results in a smaller postsynaptic current, because there is a smaller voltage driving force across the junction, and the conductance will not open as much.

An additional factor is that the current injected into the postsynaptic neuron from the second presynaptic neuron is also partially shunted through the still partially open junctions back to the first presynaptic neuron, so that the net synaptic current evoked by the second neuron's action potential is considerably smaller than that of the first. There is a period of time, determined by the membrane time constant of the postsynaptic neuron and the kinetics of the opening and closing of the voltage-dependent conductances, when the second synaptic input will be weakened by the first. The postsynaptic neuron will therefore respond optimally to precisely synchronized firing of the two presynaptic neurons. In the model presented by Edwards *et al.* [3], a delay of 250 microseconds produced a large decrease in the amplitude of the second synaptic current, and a significant decrease in the amplitude of the postsynaptic potential evoked by the summed action of the two presynaptic inputs.

Electrical coupling can increase or decrease synchrony in neuronal populations. As intuition and prevailing wisdom suggest [1], strong electrical coupling generally promotes synchrony. Less intuitively obvious is the finding that weak electrical coupling can result in a variety of alternating out-of-phase activity patterns [6–8]. Figure 3a shows a simulation of two simple and identical model neurons that are intrinsically oscillatory. Initially the two neurons are uncoupled, but fire together because the simulation was initiated simultaneously. At the first downward arrow, the neurons are weakly coupled. Over the next time period, their oscillations drift further and further out of phase, until they fire in alternation. When the coupling is increased further, they come back into phase.

When two model neurons have semi-realistic intrinsic properties, as their coupling strength is increased, there can be a quite complicated series of changes in the extent of synchrony that they display (M. Kawato, personal communication). Modulators that alter the strength of electrical synapses [1] may therefore produce significant changes in the extent of synchrony in electrically-coupled populations of cells. Additionally, when two neurons are weakly

Figure 3



Electrical coupling, synchronization and oscillations. **(a)** Two model neurons were uncoupled at the start of the simulation, but fire synchronously because the simulations were started at the same time. At the first downward arrow, the neurons were coupled weakly, and one of them given a small current pulse. Over time, the two neurons move from in-phase to out-of-phase activity. At the second downward arrow, the coupling was increased, and the two neurons synchronized again. (Modified from [7].) **(b)** When uncoupled, two model neurons are not spontaneously active, but when depolarized (upward arrow) they each generate a single burst. When weakly coupled (g = 0.1) and depolarized the neurons produce synchronous damped oscillations; when the coupling is further increased (up to g = 0.5), the neurons oscillate synchronously in the absence of depolarizing input. (Modified from [8].)

coupled, current injections can cause transitions between synchronous and alternating patterns of activity [6], suggesting that synaptic or modulatory inputs could flip networks of this sort from synchronous to asynchronous states.

Another non-intuitive finding is that electrical coupling of neurons that are not spontaneously oscillatory in isolation can result in network oscillations [8,9]. This latter case may be important for understanding how network oscillations in the pancreas and inferior olive result from coupling of a population of cells that may be primarily non-oscillatory when viewed in isolation [8,9]. Figure 3b shows the result of coupling two model neurons, neither of which spontaneously oscillates in isolation, but which fire a single burst in response to a brief depolarizing current pulse. When the neurons are weakly coupled, the network does not oscillate spontaneously but it can be triggered to do so in response to a brief depolarization. As the coupling strength is increased, the network spontaneously produces stable, large amplitude synchronous oscillations.

Oscillatory firing, transmission speed and synchronous activity are important in many contexts in the nervous system. Much further work is needed to fully elaborate the computational roles of both rectifying and non-rectifying electrical connections in neural computations.

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